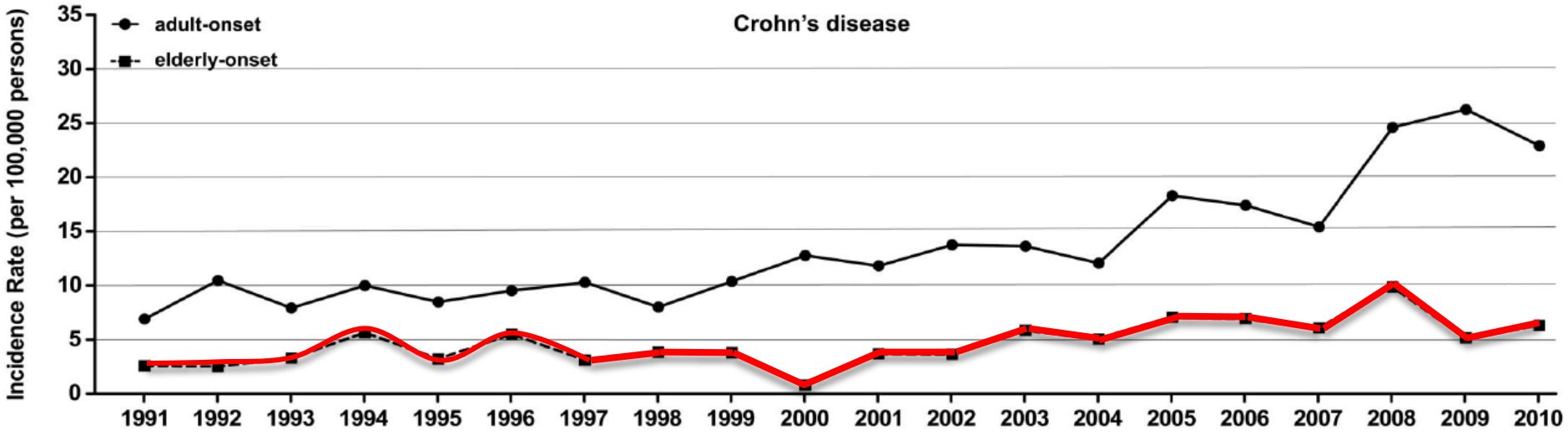
ROMA 28 novembre 01 dicembre 2018
Auditorium della Tecnica

SOCIETÀ ITALIANA DI GERONTOLOGIA E GERIATRIA

LE MALATTIE INFIAMMATORIE CRONICHE INTESTINALI NELL'ANZIANO

I nuovi farmaci biologici: anche nell'anziano?

ANNA KOHN (Roma)



Jeuring SFG, Inflamm Bowel Dis 2016

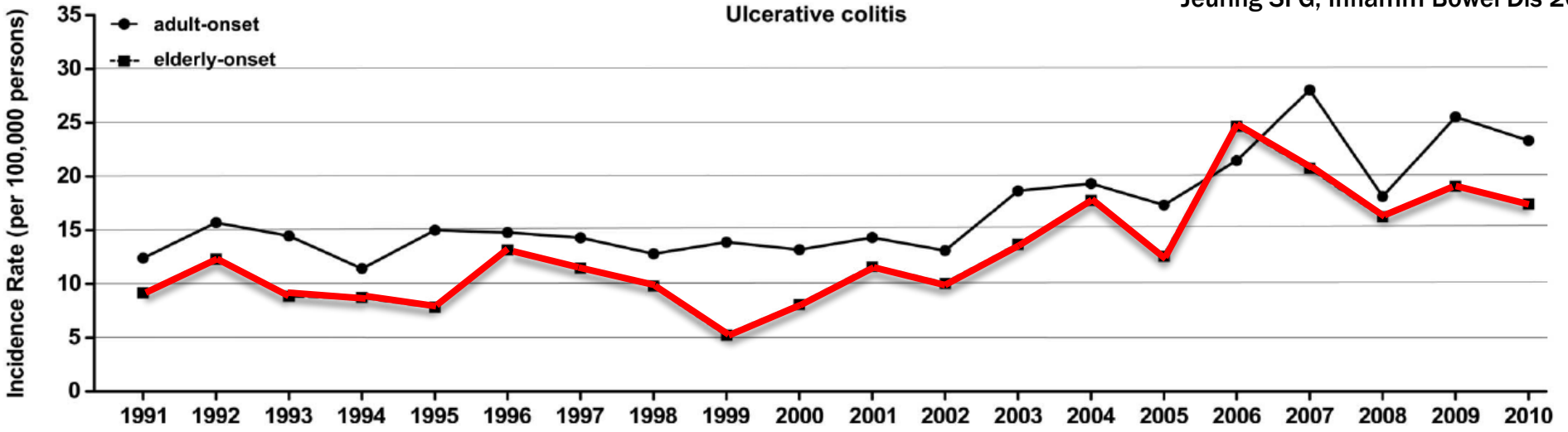
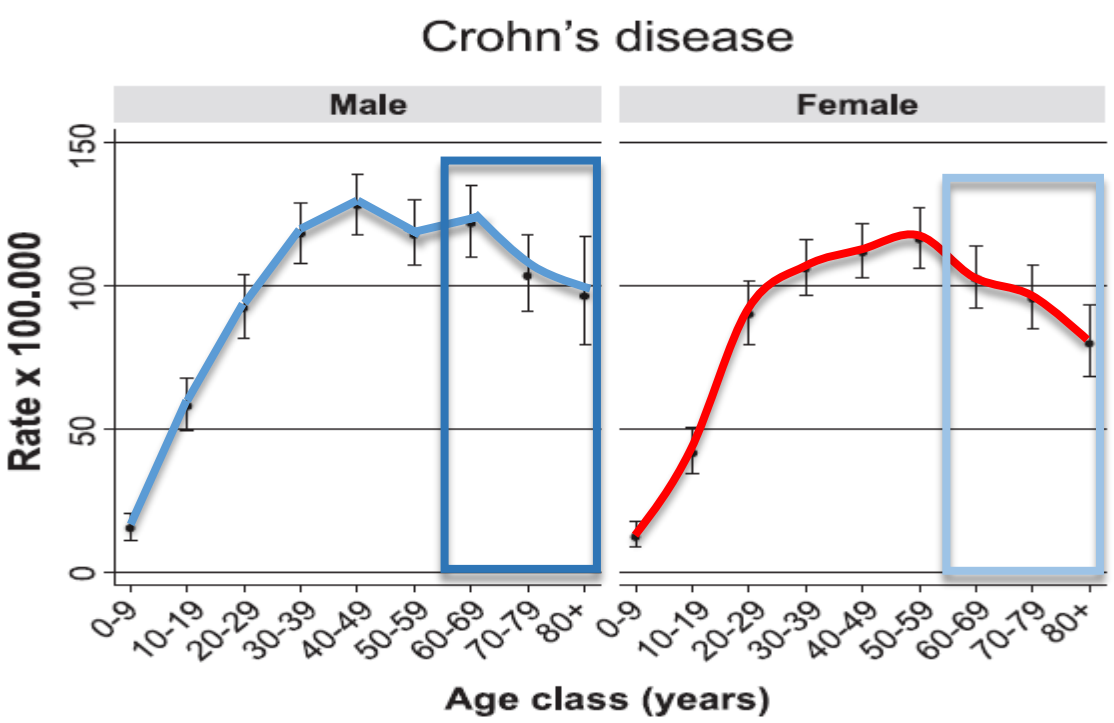


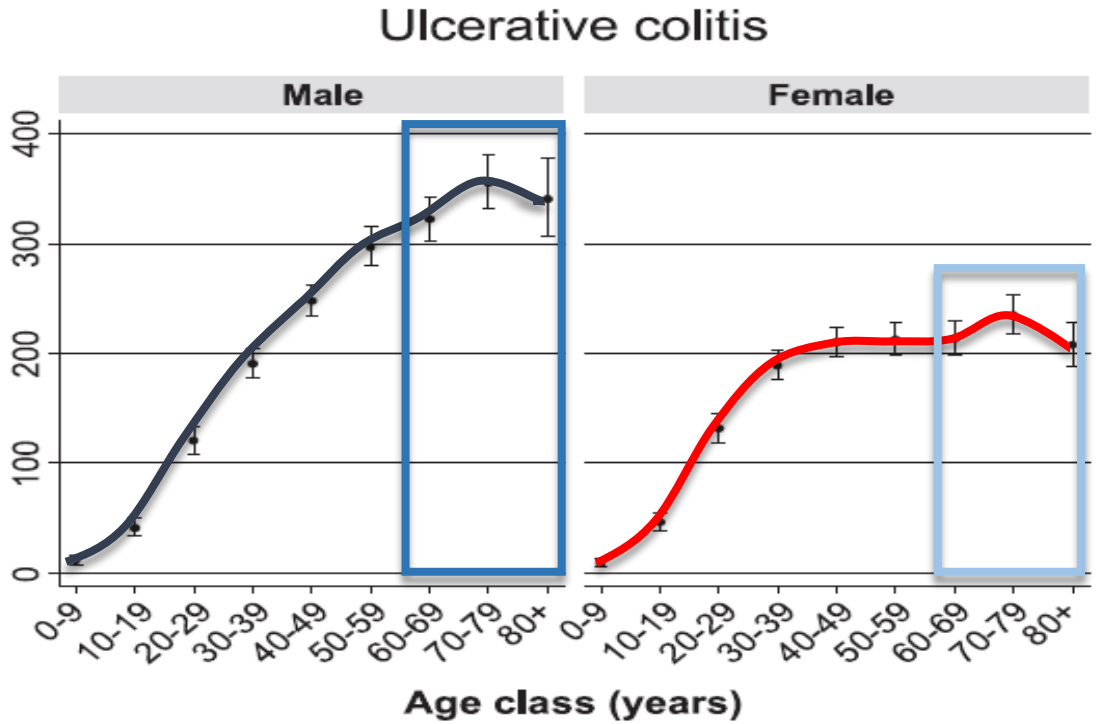
FIGURE 1. Incidence rates of AO and EO CD and UC in the South Limburg area of the Netherlands. Incidence rates were corrected for age, sex, and calendar year.

prevalence slope

IBD Prevalence on December 31,2009 in the Lazio region

Di Domenicantonio R et al, DLD 2014





Prevalence CD 91:100.000 ♂

81:100.000 ♀

144:100.000

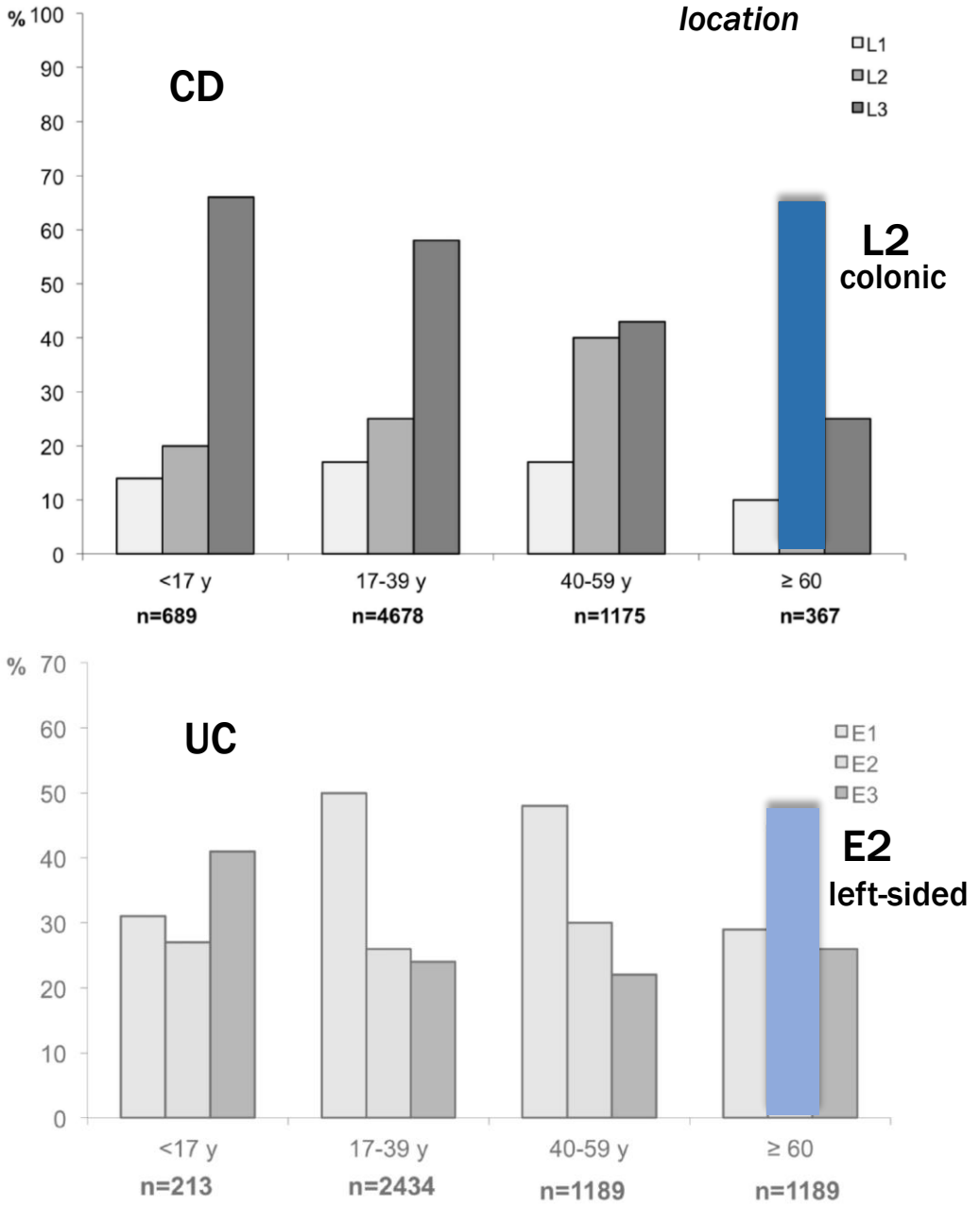
♂ 177:100.000

♀

Disease course of elderly-onset IBD

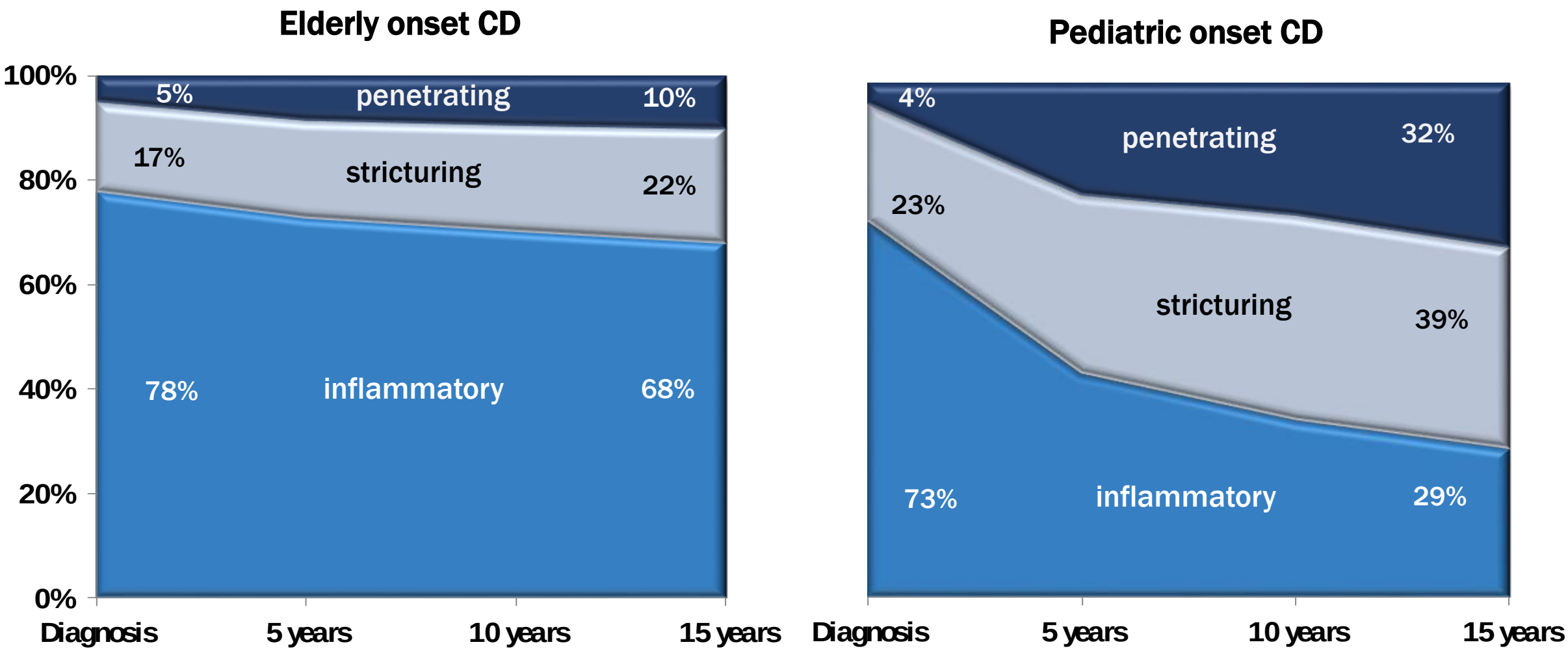
	Crohn's disease	Ulcerative colitis
location		more often left sided (E2)
symptoms	less bleeding and addominal pain	less diarrhoea, abdominal pain and weight loss
disease behaviour	mostly inflammatory	more likely stable
extraintestinal manifestations	less common	less common
cancer risk	Higher risk of NH lymphoma with thiopurine and NMSC with anti-TNF therapy	

Sturm A et al., J Crohns Colitis 2016; Taleban S et al, Dig Liver Dis 2016; Nimmonds D et al., World J Gastrointest Pharmacol Ther 2016; Butter M et al, Maturitas 2018; Everhov AH et al., Gastroenterology 2018; Ananthakrishnan AN J Crohns Colitis 2016.

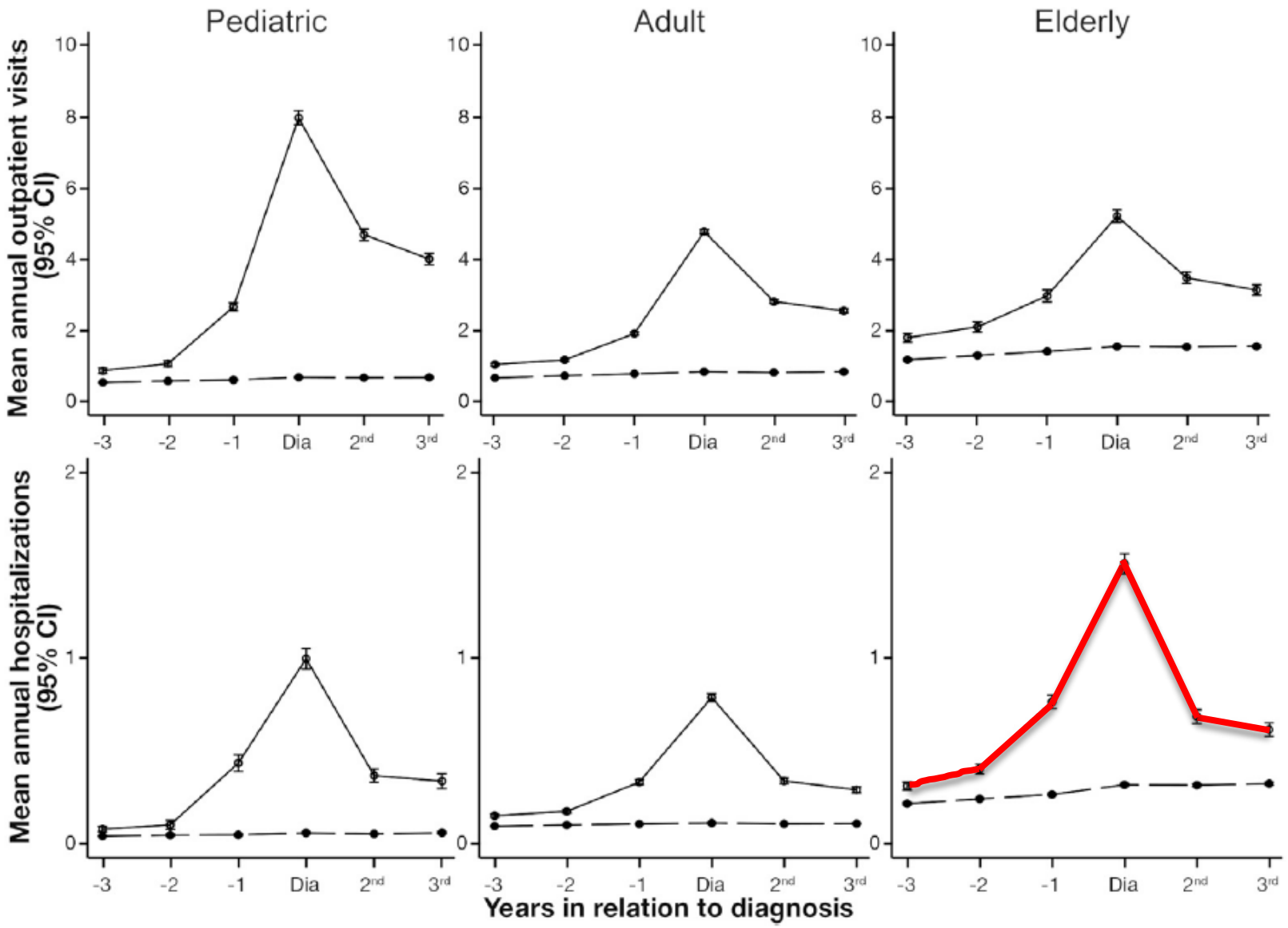


Charpentier C et al. GUT 2013

IBD Epidemiology from a French population -based registry (EPIMAD)



Gower-Rousseau C, et al. Dig Liver Dis 2013



The risk of IBD-related hospitalization is higher in elderly UC, but not CD patients, than in younger adults.

Everhov AH, Gastroenterology 2018

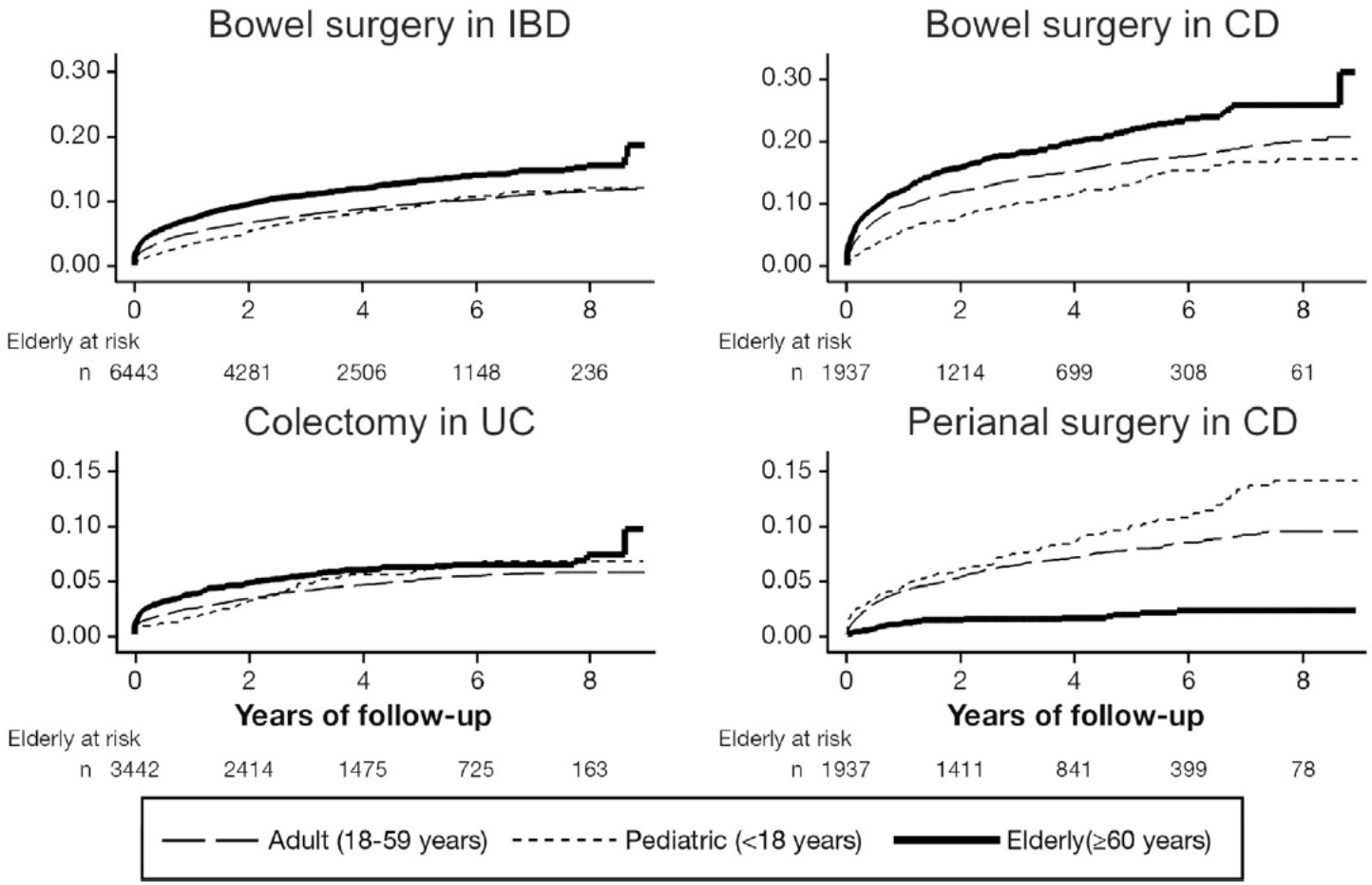
Conflicting data on the risk of surgery for the elderly IBD.

Study based on administrative data report an increased risk due to a mixed population of elderly with long standing IBD and elderly onset IBD.

Everhov AH et al., Gastroenterology 2018
Nguyen GC Inflamm Bowel Dis 2017

No difference in surgery risk was observed by population-based study

Jeuring FSG et al; Inflamm Bowel Dis 2016
Lakatos PL et al.; J Crohns Colitis 2011



Everhov AH, Gastroenterology 2018

IBD related surgery: postsurgical mortality and complications

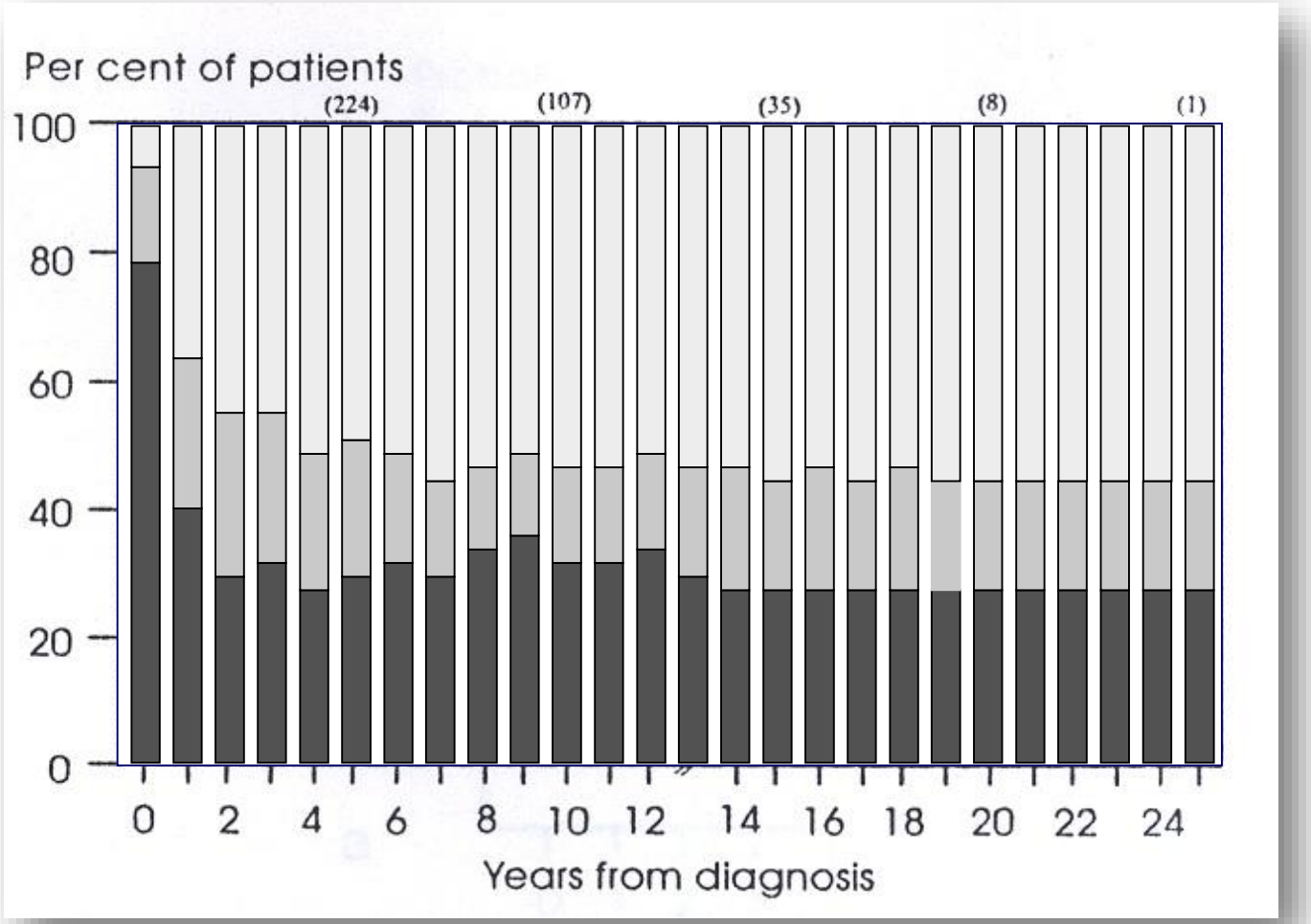
	Crohns		Ulcerative colitis	
	elderly	non elderly	elderly	non elderly
30-day mortality	4.2	03 **	6.1	0.7**
infectious complications	16.2	13.6	24.7	16**
cardiac complications	2.3	0.2**	2.6	0.3**
renal complications	2.2	0.6**	3.1	1.2**
neurologic complications	0.5	0.1*	1.0	0.2**
venous thromboembolism	3.1	1.5**	4.1	3.3

* p<0.05 ** p< 0.01, *** p< 0.001

Bollegala N et al.; Clin Gastroenterol Hepatol 2015

elderly patients undergoing IBD-related bowel surgery experience a pronounced 5- to 10-fold higher 30-day mortality than younger IBD patients, as well as number of other systemic complications

Crohn's disease: Disease activity distribution in each year from diagnosis



55%
remission

15%
low activity

30%
high activity

Munkholm P et al., Scand J Gastro 1995 P

ECCO Current Practice Position 8

There is no evidence that the efficacy of medical treatment in elderly IBD patients differs from that in younger adult patients

ECCO Current Practice Position 9

All available data indicate a higher risk of serious adverse events with prolonged use of corticosteroids in elderly patients with IBD when compared to younger adult patients

ECCO Current Practice Position 11

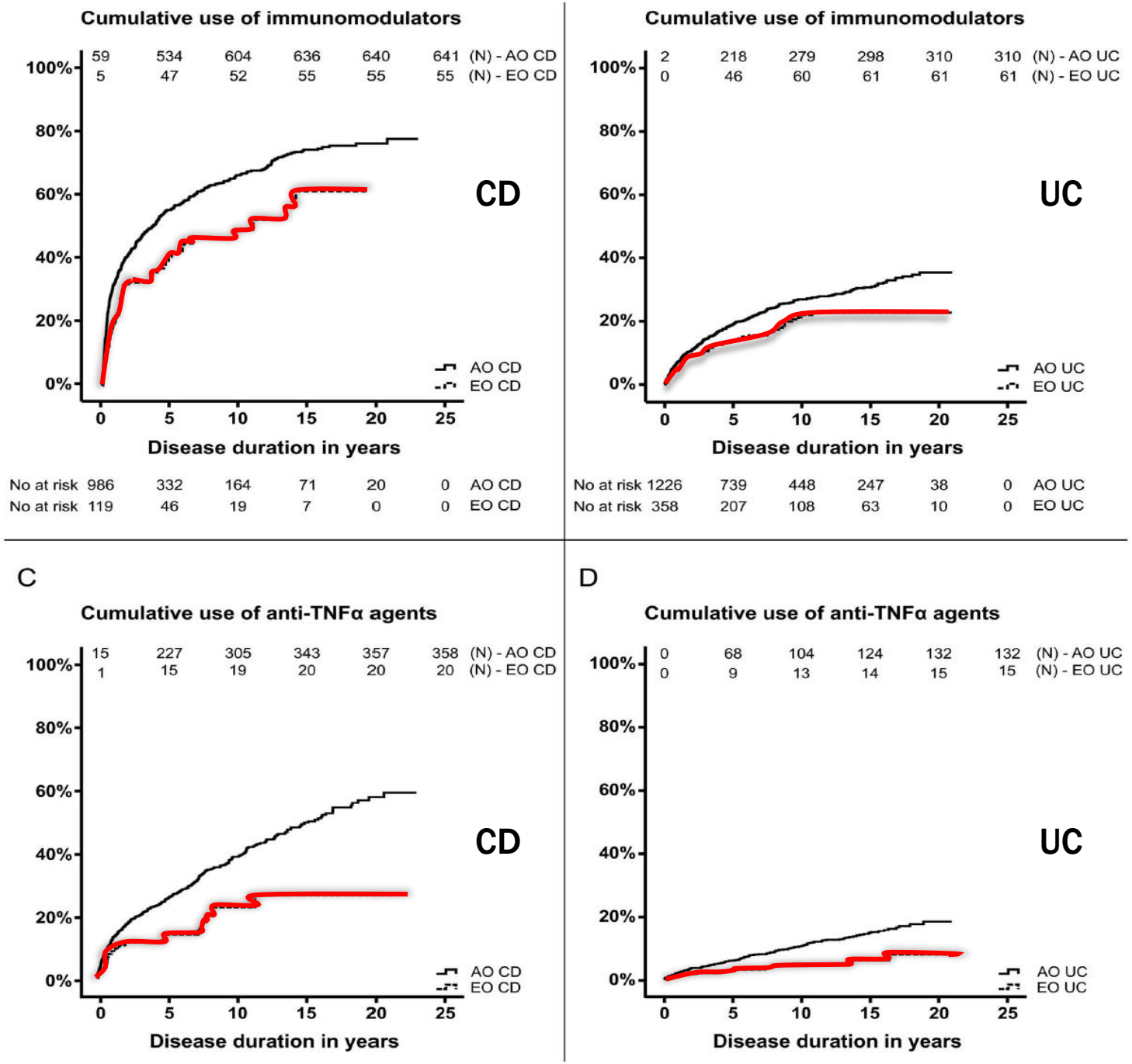
Elderly IBD patients treated with TNF inhibitors for IBD have an increased risk of severe infection compared with younger patients

ECCO Topical Review

European Crohn's and Colitis Organisation Topical Review on IBD in the Elderly

Andreas Sturm,[a] Christian Maaser,[b] Michael Mendall,[c] Dimitrios Karagiannis,[d] Pantelis Karatzas,[e] Nienke Ipenburg,[f] Shaji Sebastian,[g] Fernando Rizzello,[h] Jimmy Limdi,[i] Konstantinos Katsanos,[j] Carsten Schmidt,[k] Steven Jeuring,[l] Francesco Colombo,[m] Paolo Gionchetti[n]

Sturm A et al., J Crohns Colitis 2016



ongoing treatments

The elderly are less likely to receive biological agents or IMM. This may be secondary to concerns for risks for infection and cancer; or may reflect that the elderly do have more comorbidities and polypharmacy making the use of more medications riskier.

Jeuring FSG et al.,Inflamm Bowel Dis 2016

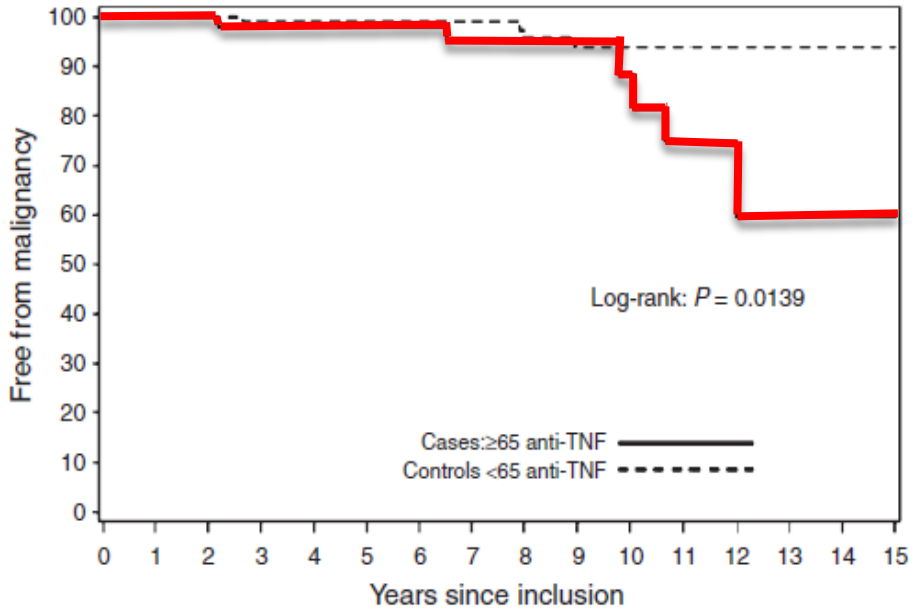
Advanced Age Is an Independent Risk Factor for Severe Infections and Mortality in Patients Given Anti–Tumor Necrosis Factor Therapy for Inflammatory Bowel Disease

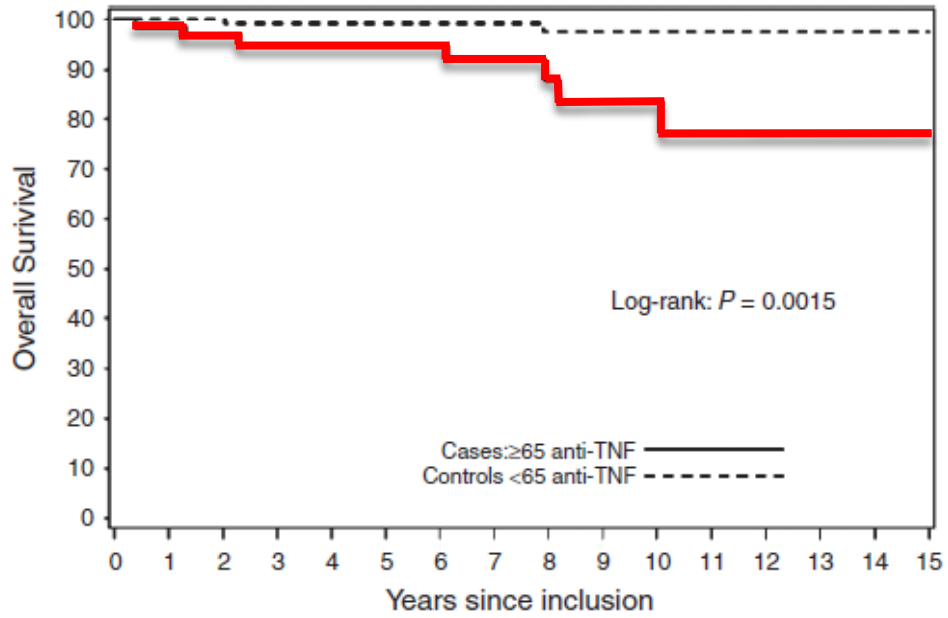
MARIO COTTONE,* ANNA KOHN,‡ MARCO DAPERNO,§ ALESSANDRO ARMUZZI,‖ LUISA GUIDI,‖ RENATA D'INCA,¶ FABRIZIO BOSSA,# ERIKA ANGELUCCI,** LIVIA BIANCONE,‡‡ PAOLO GIONCHETTI,§§ SANDRO ARDIZZONE,‖‖ CLAUDIO PAPI,¶¶ WALTER FRIES,## SILVIO DANESE,*** GABRIELE RIEGLER,‡‡‡ MARIA CAPPELLO,§§§ FABIANA CASTIGLIONE,‖‖‖ VITO ANNESE,# and AMBROGIO ORLANDO*

IG IBD
the Italian Group for the study of Inflammatory Bowel Disease

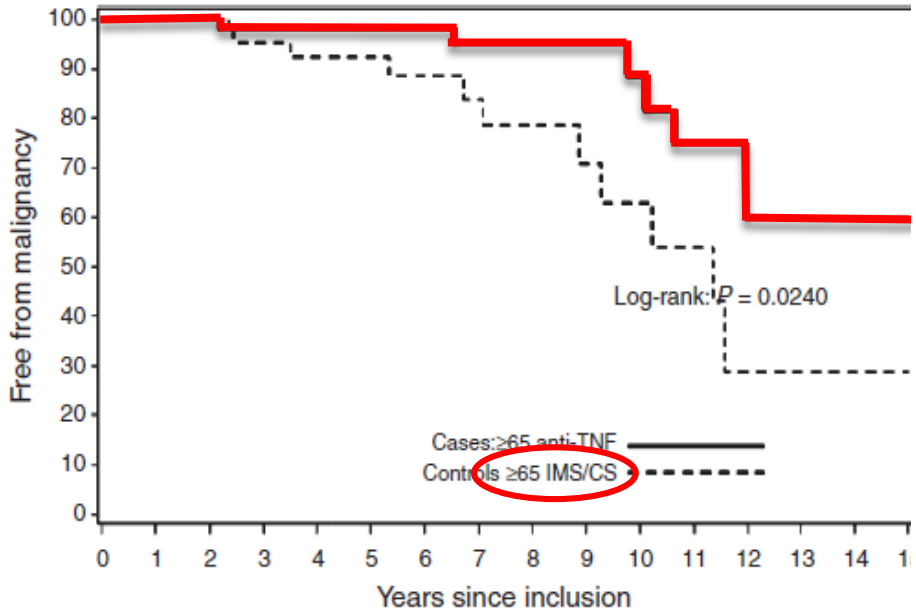
	95 elderly patients treated with biologics		190 adult matched controls treated with biologics		190 elderly controls not treated with biologics	
	UC	CD	UC	CD	UC	CD
Pts n°	37	58	74	116	74	116
Male/female	20/17	35/23	40/34	70/46	40/34	70/46
Mean age(range)	71 (65-81)	71(65-84)	38(17-64)	39(16-64)	71(65-81)	70(65-80)
Remission n° (%)	22 (59.5)	38 (65.5)	42(56.7)	68 (58.6)	-	-
Maintenance n° (%)	12 (32.4)	39 (67.2)	24 (32.4)	78 (67.2)	-	-
Comorbidity n° (%)	35 (94.5)	44 (75.8)	4 (5.4)	6 (5.1)	37 (50)	46(39.6)
Deaths (n°)	4	6	0	2	2	3
Severe infections (n°)	5	6	2	3	1	0
Cancer (n°)	1	1	0	0	1	3
Steroids (n°)	36	54	72	108	74	104
antiTNF+AZA/MTX n° (%)	7 (19)	15 (26)	17 (23)	32 (28)	-	-

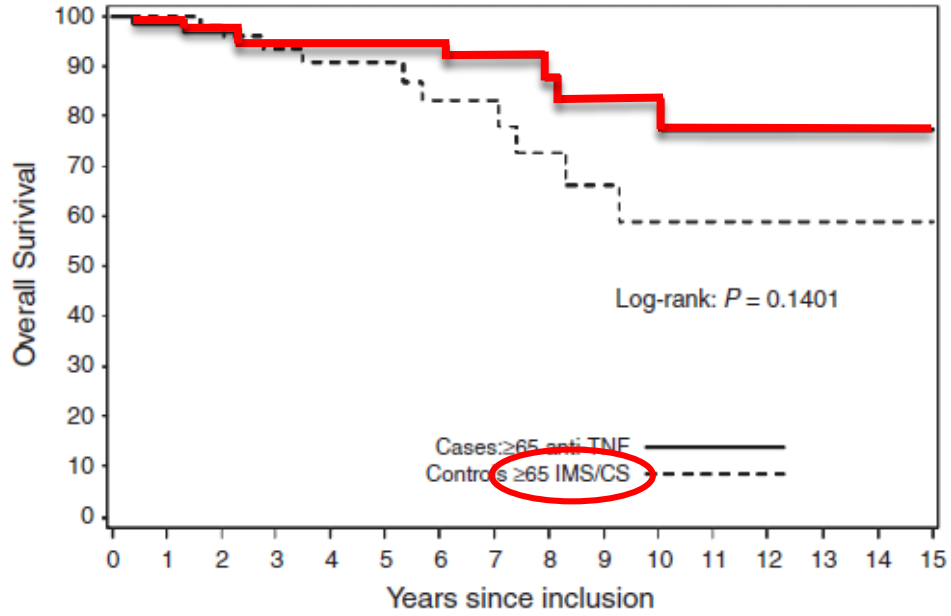
M Cottone et al., Clin Gastroenterol Hepatol 2010



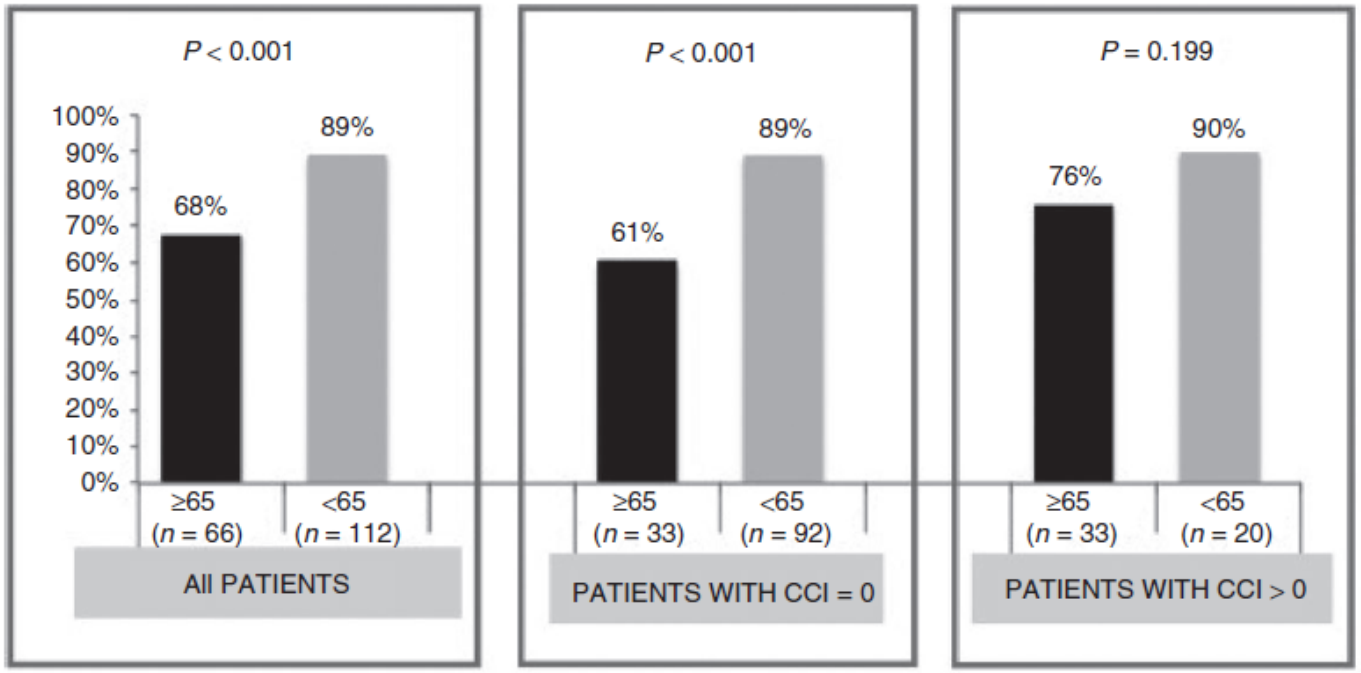


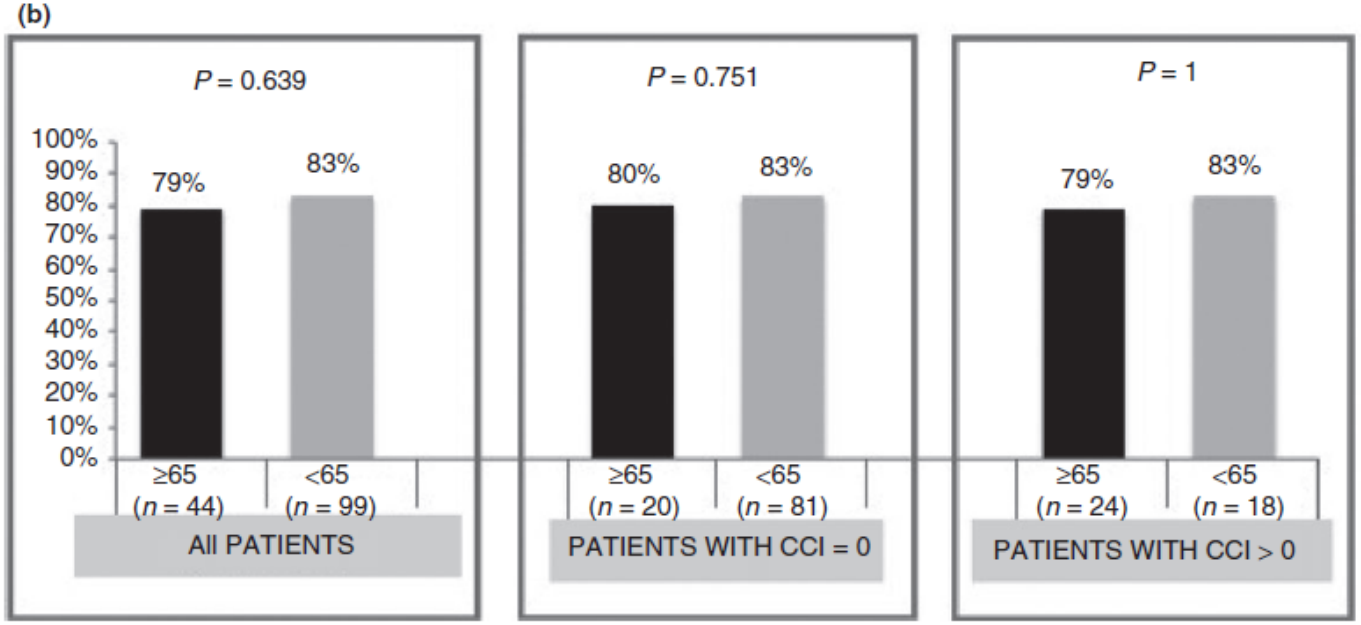
Malignancy and mortality during the follow up in IBD cases: ≥ 65 yrs anti TNF as compared with controls





Lobaton T et al., Aliment Pharmacol Ther 2015





Efficacy of anti-TNF therapy

Clinical response at short term (10 weeks)
&
Clinical response at long term (≥ 6 months)

Elderly (cases)

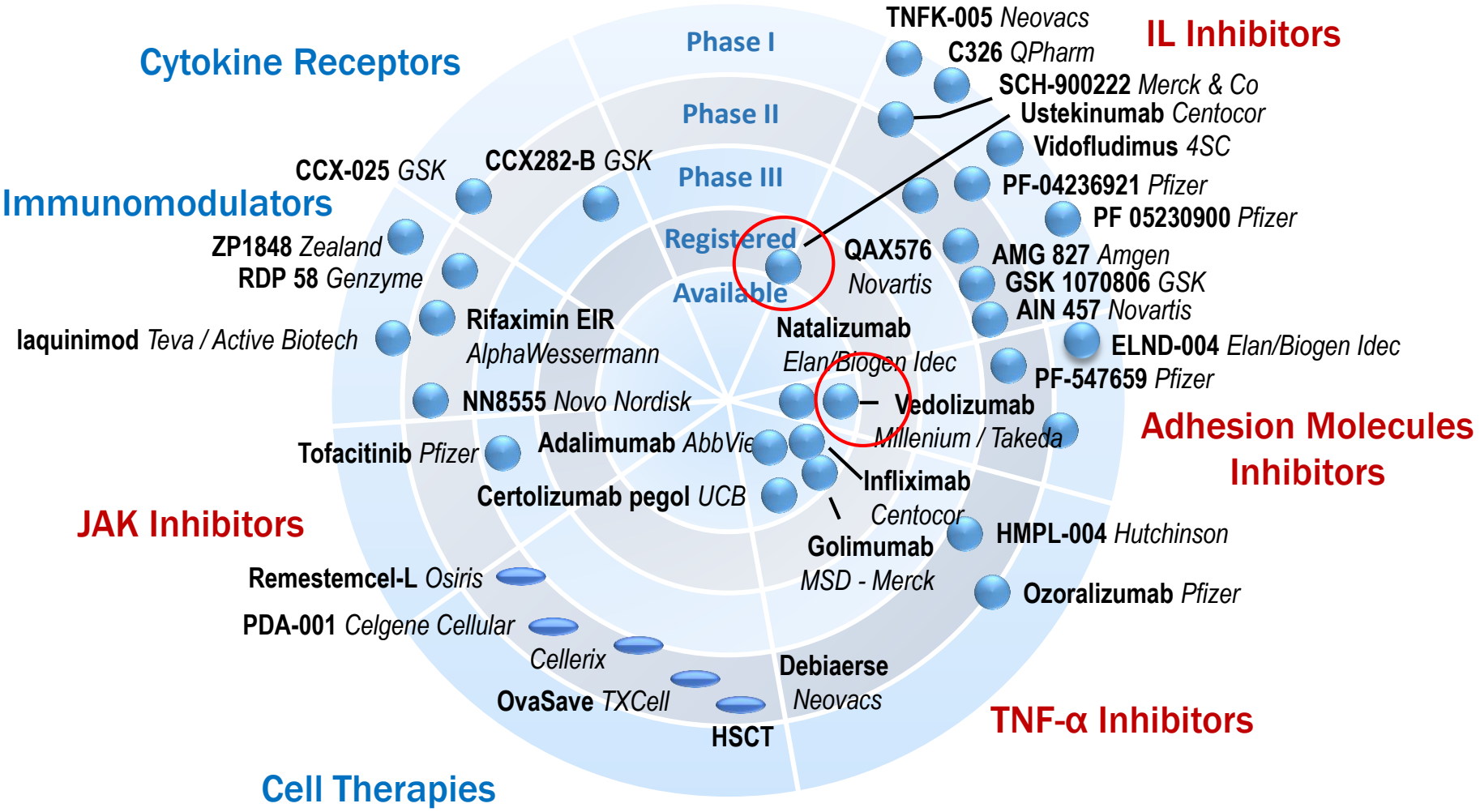
≥ 65 years

Young (control 1)

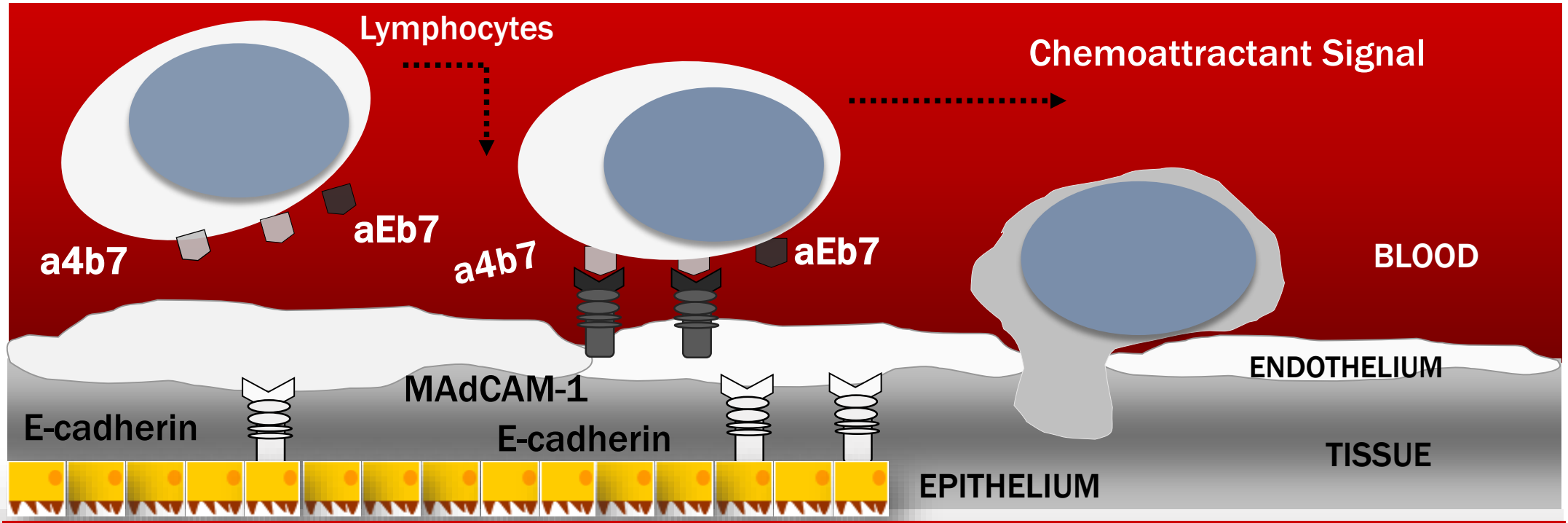
< 65 years

Lobaton T et al., Aliment Pharmacol Ther 2015

Therapeutic Galaxy in IBD

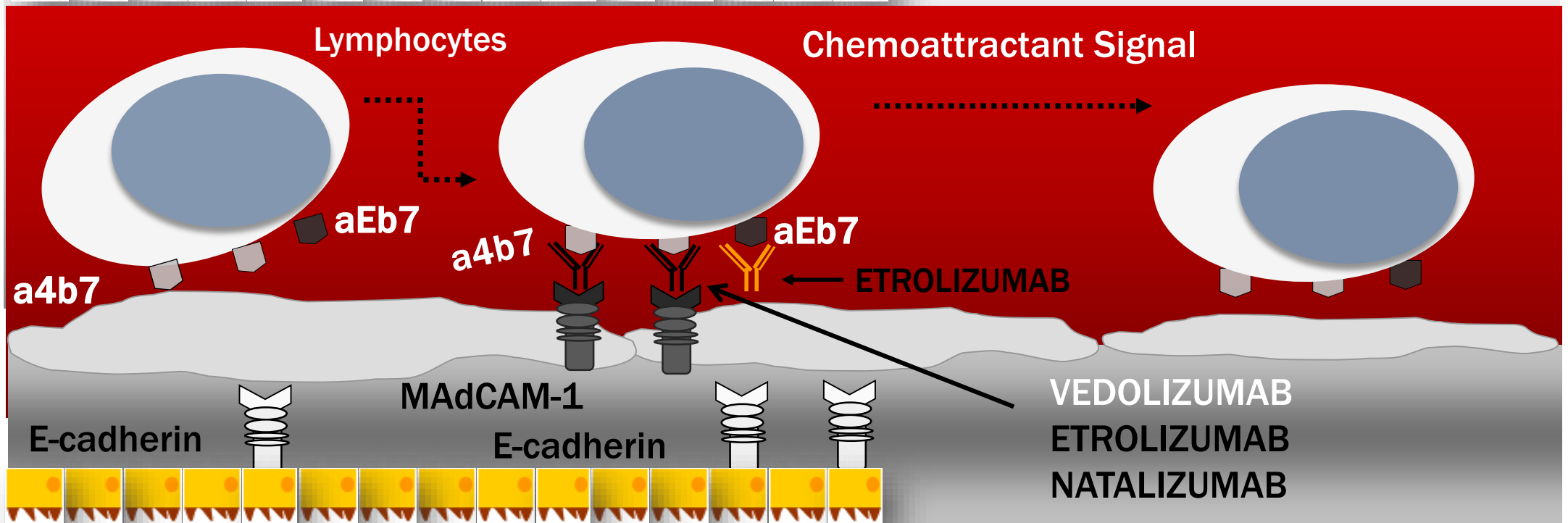


Adapted from Danese S. *Gut* 2012;61:918–32



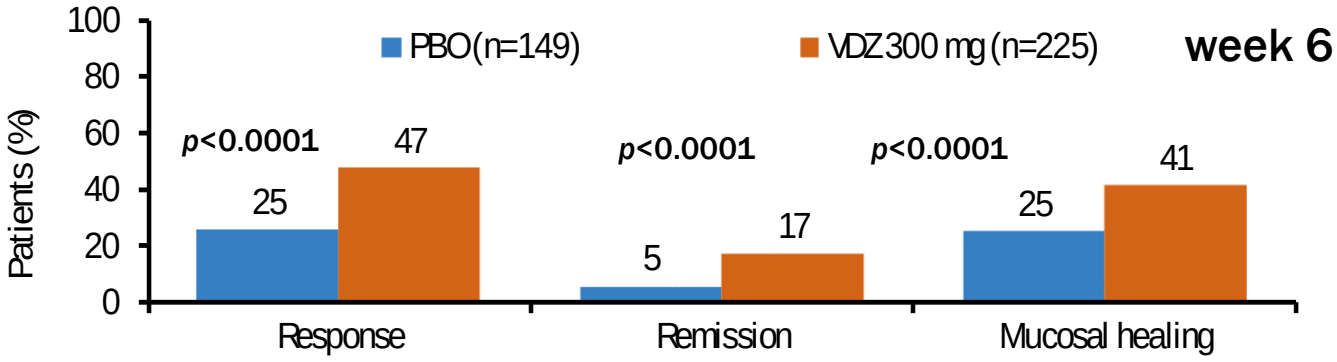
anti-adhesion therapies

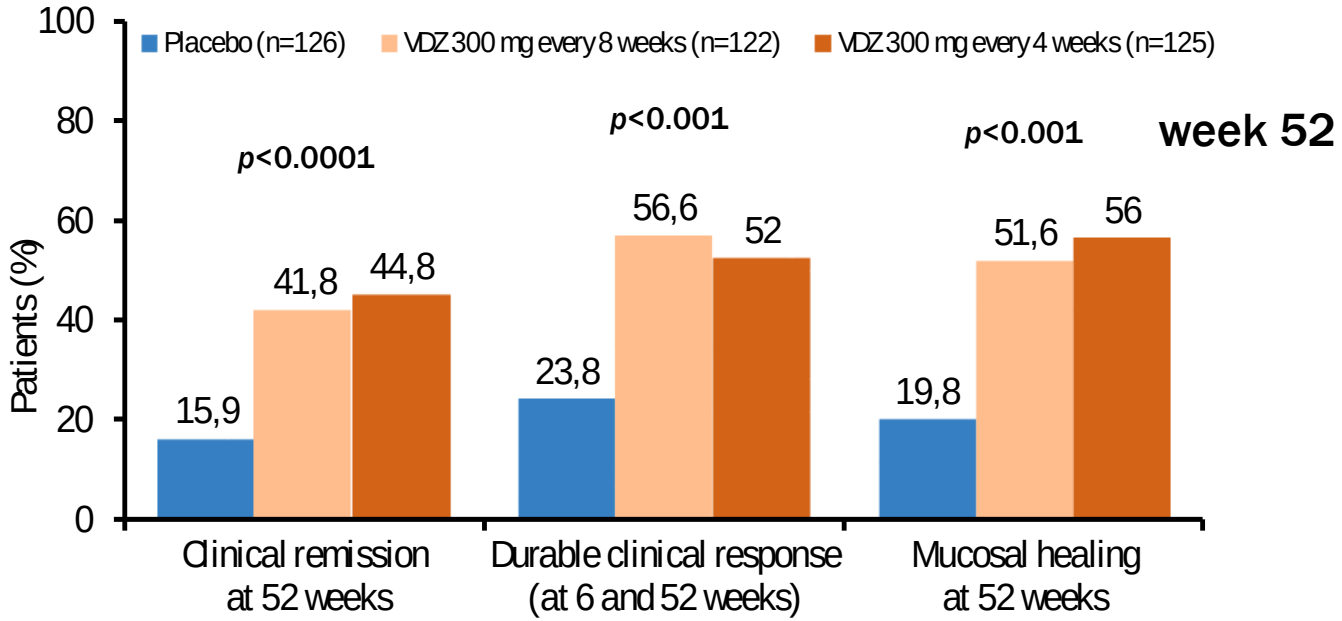
Lymphocytes Migration and retention of T cells in Gut mucosal tissue

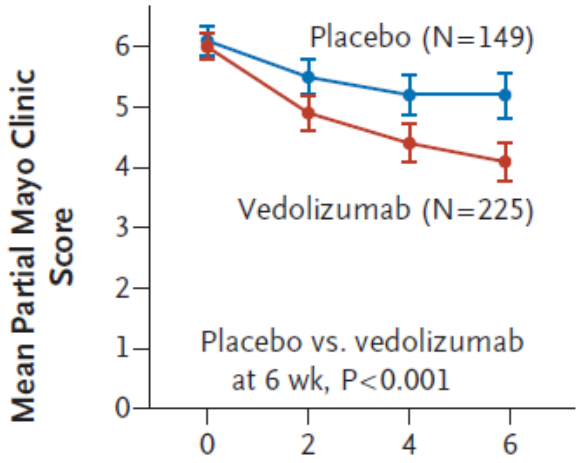


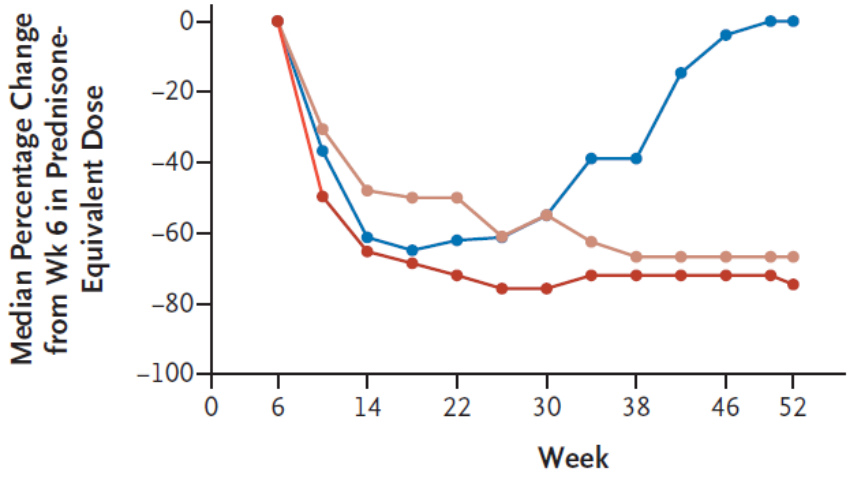
Reduced Lymphocyte Migration & Inhibition of Homing of Lymphocytes to the Gut

Vedolizumab induction and remission in moderate to severe UC- GEMINI I





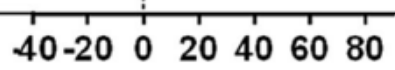




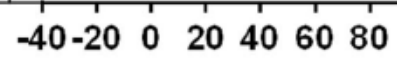
Feagan BG, *et al.* , *New J Med* 2013

Efficacy of Vedolizumab in UC and CD patients stratified by age: from the GEMINI trials

UC Age, y	UC patients in clinical response at week 6, n/N (%) PBO	 VDZ	Difference from PBO, % (95% CI)
<35	11/53 (20.8)	44/86 (51.2)	30.4 (15.2, 45.6)
35 to <55	25/78 (32.1)	50/107 (46.7)	14.7 (0.7, 28.7)
≥55	2/18 (11.1)	12/32 (37.5)	26.4 (-2.5, 52.6)



CD Age, y	CD patients with enhanced clinical response at week 6, n/N (%) PBO	 VDZ	Difference from PBO, % (95% CI)
<35	21/67 (31.3)	31/111 (27.9)	-3.4 (-17.3, 10.5)
35 to <55	14/63 (22.2)	32/96 (33.3)	11.1 (-2.8, 25.1)
≥55	3/18 (16.7)	6/13 (46.2)	29.5 (-6.4, 60.6)



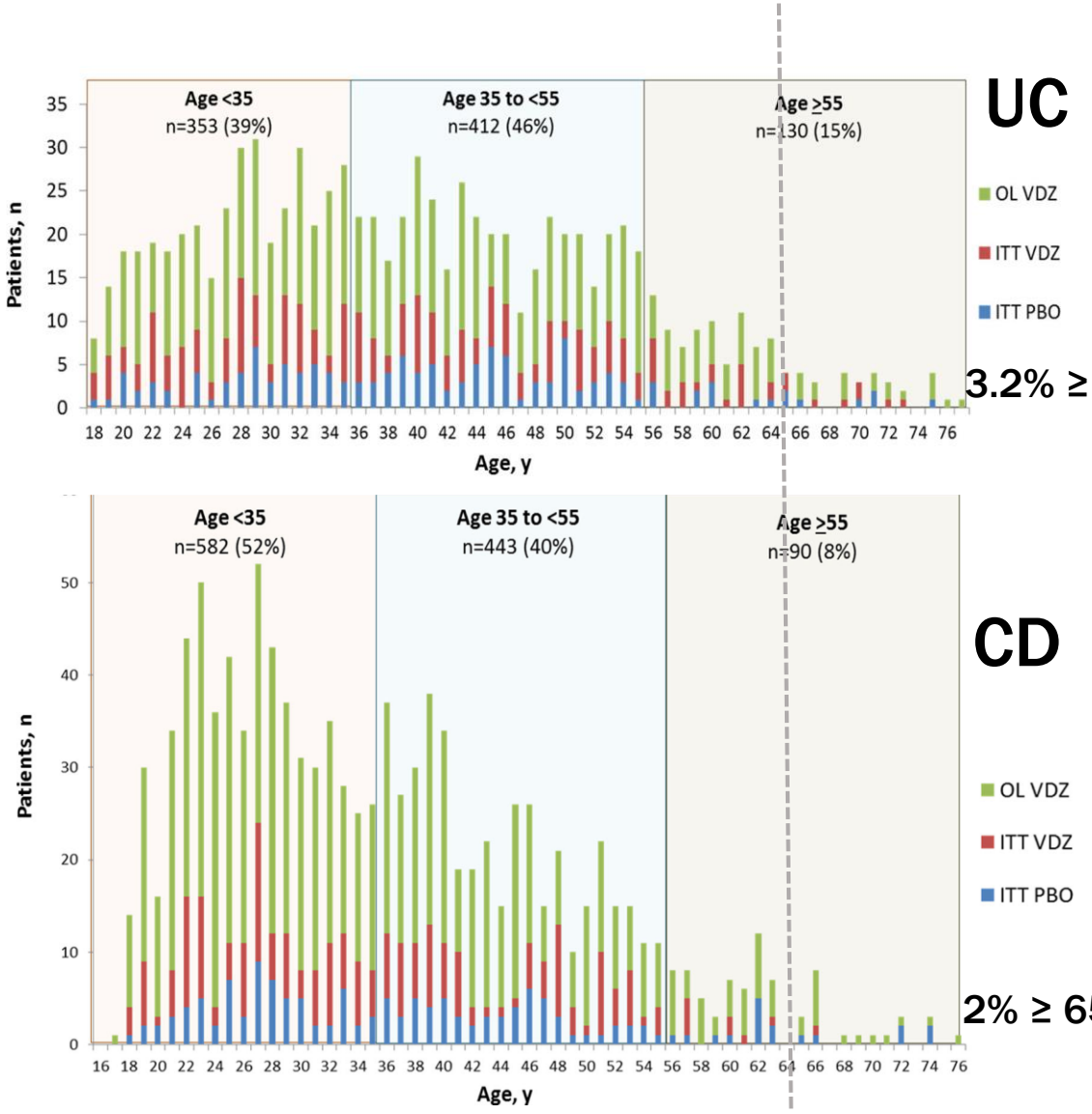
Age, y	UC patients in clinical remission at week 52, n/N (%) VDZ/PBO[a]	 VDZ/VDZ[b]	Difference from PBO, % (95% CI)
<35	10/54 (18.5)	34/101 (33.7)	15.1 (1.3, 29.0)
35 to <55	6/50 (12)	58/110 (52.7)	40.7 (27.8, 53.7)
≥55	4/22 (18.2)	15/36 (41.7)	23.5 (-3.2, 47.8)

Age, y	CD patients in clinical remission at week 52, n/N (%) VDZ/PBO[a]	 VDZ/VDZ[b]	Difference from PBO, % (95% CI)
<35	15/73 (20.5)	65/173 (37.6)	17.0 (5.3, 28.8)
35 to <55	13/65 (20.0)	42/112 (37.5)	17.5 (4.3, 30.7)
≥55	5/15 (33.3)	9/23 (39.1)	5.8 (-26.5, 37.6)

Yajinik V et al., Adv Ther 2017

safety

Adverse events by age
< 65 years and ≥ 65 years

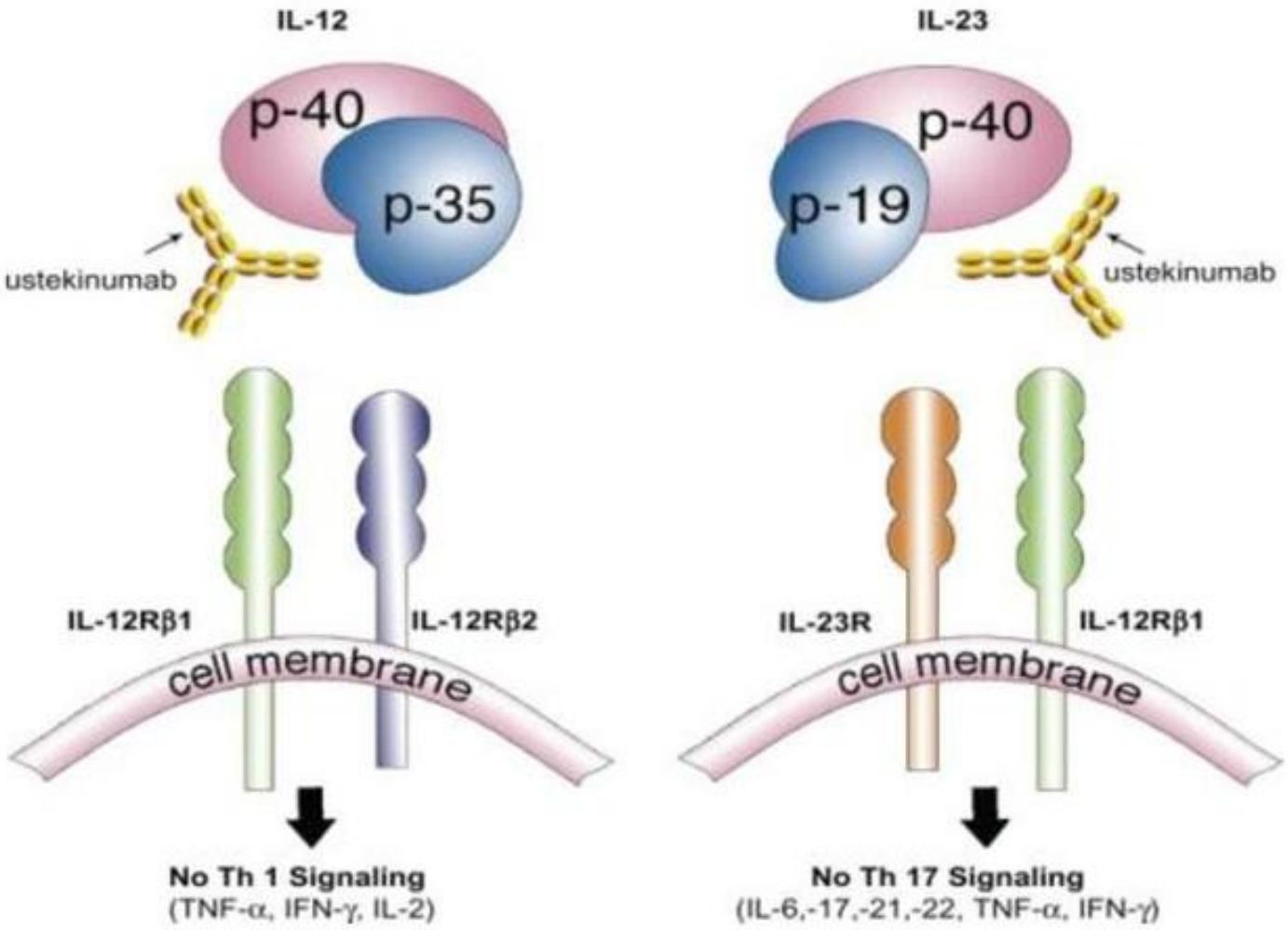


Adverse event[a]	Patients, n (%)			
	Age <65 years		Age ≥65 years	
	PBO/PBO[b] (n = 284)	VDZ/VDZ[c] (n = 1400)	PBO/PBO[b] (n = 13)	VDZ/VDZ[c] (n = 34)
Nasopharyngitis	19 (7)	177 (13)	2 (15)	3 (9)
Headache	28 (10)	171 (12)	4 (31)	6 (18)
Crohn's disease	33 (12)	161 (12)	3 (23)	3 (9)
Arthralgia	26 (9)	158 (11)	3 (23)	8 (24)
Pyrexia	21 (7)	127 (9)	1 (8)	0
Nausea	22 (8)	126 (9)	1 (8)	2 (6)
Dizziness	7 (2)	45 (3)	1 (8)	3 (9)
Edema peripheral	9 (3)	35 (3)	3 (23)	3 (9)

PBO, placebo; VDZ, vedolizumab.
[a]Only adverse events occurring in ≥9% of vedolizumab-treated patients in any group are listed.
[b]Patients received PBO during induction and maintenance periods.
[c]Patients received VDZ during induction and maintenance periods.

from the Gemini 1 and 2 trials

Yajinik V et al., Adv Ther 2017



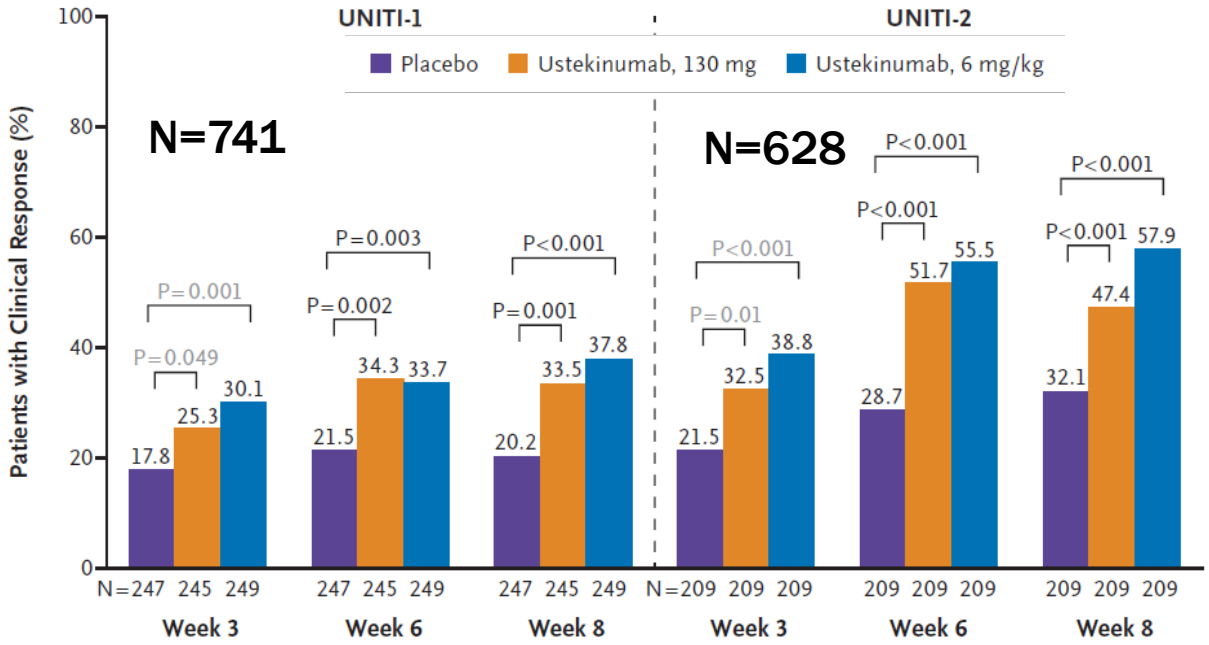
IL-12 and IL-23 pro-inflammatory cytokines sharing p40 subunit

Ustekinumab

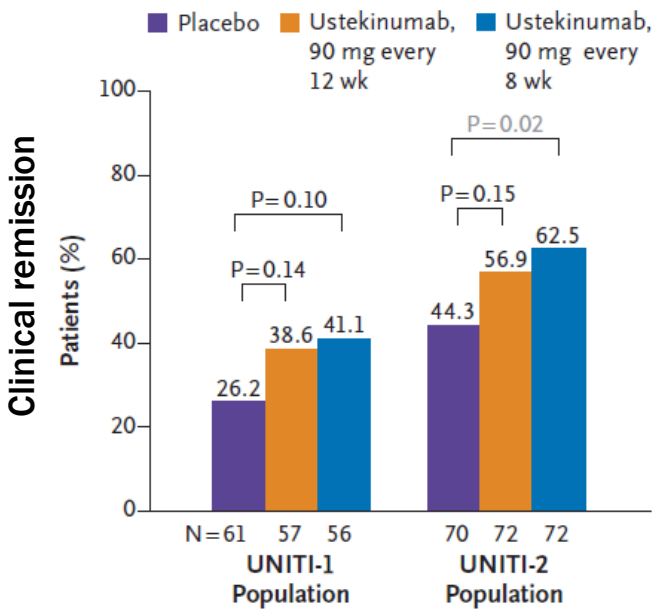
Koutruba L et al.,Ther Clin Risk Manag 2010

Ustekinumab for Crohn's Disease

8 weeks

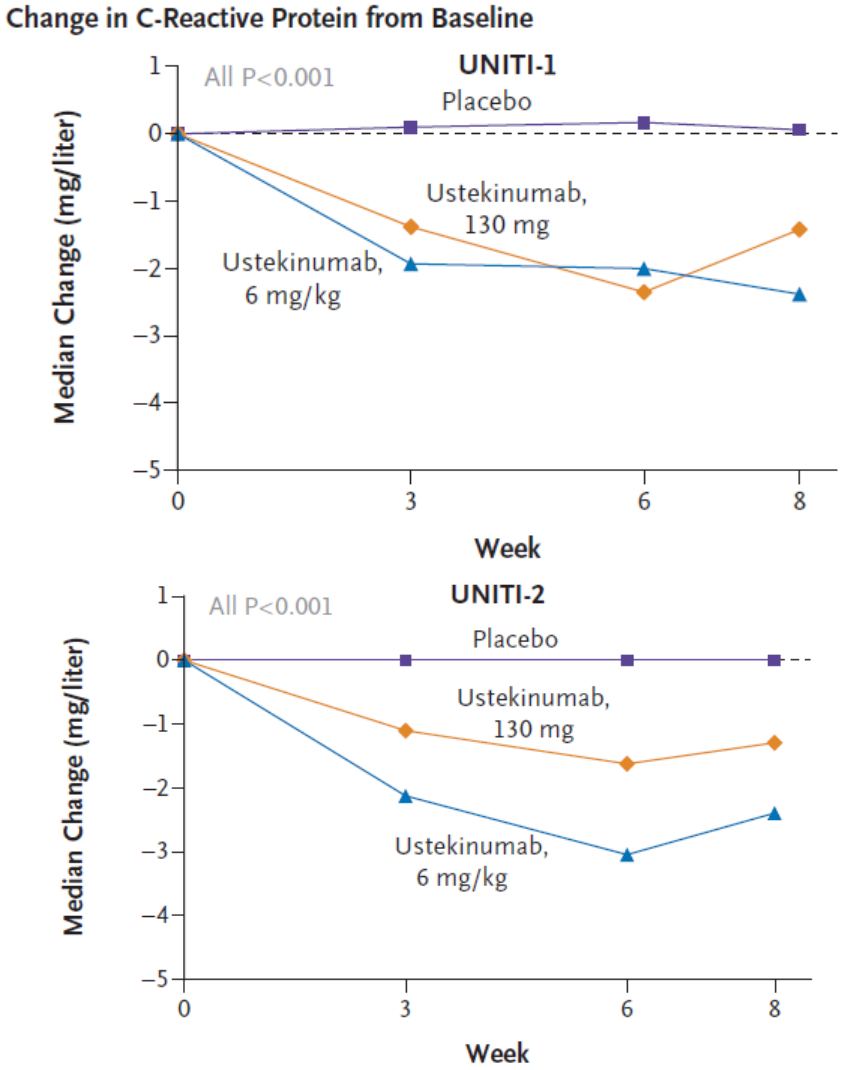


44 weeks



i.v. Ustekinumab induces response and remission in patients with moderately to severely active CD refractory to anti-TNF or conventional therapy.

s.c. Ustekinumab maintained remission in patients who had clinical response to induction therapy.



Feagan BG et al., N Engl J Med 2016

TNF inhibitors
IFX, ADA, GOLIMUMAB
UC & CD

Fast onset

Loss of response in 1/3 of cases

Very effective on EIM

Increased risk of severe infection in elderly IBD

Infusion related reactions (iv), opportunistic infections, melanoma, NMSC,demyelinatin disorders, psoriasis, aggravation of heart failure*

Rarely, non infectious hepatitis & reduced blood cells count

Increased risk of severe infection in elderly IBD

Chest X-ray, TB skin tests,IFN- Y-release assay (Quantiferon), HBV testing

Inactivated trivalent influenza vaccine, Pneumococcal vaccine (PCV 13)

Cardiological and neurological evaluation

Integrin inhibitors
Vedolizumab
UC & CD

Delayed therapeutic effect

Persistent efficacy

Moderately effective on EIM

Suitable for UC patients at risk of infections as first line

Nasopharyngitis

Infusion related reactions, psoriasis (uncommon)

Favorable safety profile
Limited data in the elderly

Chest X-ray, TB skin tests,IFN- Y-release assay (Quantiferon), HBV testing

Inactivated trivalent influenza vaccine, Pneumococcal vaccine (PCV 13)

Anti IL12 -IL 23 mab
Ustekinumab
CD

Fast onset

Persistent efficacy

Effective on EIM

Suitable for CD patients at risk of infections as first line

Nasopharyngitis

Infusion related reactions (uncommon)

Favorable safety profile
no data in the elderly

Inactivated trivalent influenza vaccine, Pneumococcal vaccine (PCV 13)

when making management decisions in the elderly IBD

“ageism” should be avoided

focus on functional status and comorbidities

avoid emergent surgeries

more frequent clinical assessment